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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/884,875	06/18/2001	Lin-feng Chen	UCAL-234	1891

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EXAMINER	
LEFFERS JR, GERALD G	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 12/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/884,875	CHEN ET AL.	
	Examiner	Art Unit	
	Gerald G Leffers Jr., PhD	1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 23 November 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 2 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☒ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *1-10 and 19-31*.

   Claim(s) objected to: _____.

   Claim(s) rejected: *32-42*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Gerald G Leffers Jr., PhD
Primary Examiner
Art Unit: 1636

Advisory Action Attachment

Continuation of 2. NOTE: The amendment of claim 38 to recite "contacting the cell with an anti-acetylated lysine antibody" raises new issues under 35 USC 112 1st paragraph (e.g. for comprising NEW MATTER), and also changes the scope of the recited method, requiring a new search. For example, the instant specification discloses the use of the specifically recited "anti-acetylated lysine antibody" only in the context of a Western blot where the acetylated RelA was obtained by immunoprecipitation with a different antibody specific for a T7 tag fused to RelA. Therefore, there does not appear to be literal or inherent support for the use of an anti-acetylated lysine antibody as recited in the proposed amendment. At a minimum, the proposed amendment of the claims would require searching the art for other proteins within mammalian cells that might be identified by an anti-acetylated lysine antibody as used in the proposed method of claim 38 (e.g. with regard to enablement).

Continuation of 5. does NOT place the application in condition for allowance because:

Arguments directed to the amended claims are moot as the proposed amendment of the claims has not been entered.

With regard to arguments directed to the rejection of claims 32-37 for comprising impermissible NEW MATTER in claiming the use of a broad genus of nuclear export inhibitors, applicants' arguments are found to be nonpersuasive. The response is correct to note that HDAC3 is actually an activator of RelA export from the nucleus and that the instant specification teaches two compounds that can function to inhibit nuclear export, trichostatin A (i.e. TSA, an inhibitor of HDAC3 activity) and leptomycin B. In fact, in the working example

provided by applicants, HDAC3 can be considered as the "candidate agent" that is brought into "contact" with the host cell and assessed for its ability to modulate the presence of RelA in the cell. Applicants' response argues that the specification teaches at least two embodiments of the claimed invention where TSA and/or leptomycin B is used to inhibit export of RelA and in which the amount of deacetylated RelA is determined (i.e. using a GFP-RelA fusion whose cellular location is determined by flourescence). Applicants' response further argues that one of skill in the art would necessarily recognize that other inhibitors of nuclear export are and were known in the art (e.g. the teachings of Finlay et al and Pasquinelli et al) and would recognize that applicants were in possession of the broadly claimed invention.

Applicants' arguments are not persuasive in that the rejection is a new matter rejection and a single working example where two different export inhibitors are used cannot be considered as providing descriptive support for claiming the broadly recited method of the rejected claim. There is no convincing evidence of record in the originally filed specification or claims that applicants considered the broadly recited method of blocking nuclear export and measuring nuclear levels of deacetylated RelA as their invention. There is no generic teaching for this concept. Rather, a single example is taught where the effects of HDAC3 activity on regulation of NF-kB activity are assessed. In this working example, TSA is not even explicitly taught as an agent that globally "blocks nuclear export", as is recited in the rejected claims. Further, the single working example is directed to a single cell type (i.e. HeLa cells) and utilizes a single technique for determining the level of deacetylated RelA in the nucleus of the transformed cells (i.e. flourescence microscopy detecting the cellular distribution of a GFP-RelA fusion protein). In the absence of a more generic teaching from the instant specification for the

broadly recited method, there is no support in the originally filed specification for the method as recited in the rejected claims. The single working example provided in the originally filed specification at most provides descriptive support for the method as performed in the working example itself (i.e. where HDAC3 is the candidate agent, TSA and/or leptomycin B is the nuclear export blocking agent and a GFP-RelA fusion is recombinantly expressed in HeLa cells).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gerald G Leffers Jr., PhD
Primary Examiner
Art Unit 1636

ggl

GERRY LEFFERS
PRIMARY EXAMINER